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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/966,233	11/07/1997	SE-JIN LEE	241800	5193

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EXAMINER
ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
1631	22

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/966,233	Applicant(s) LEE, SE-JIN	
	Examiner Marjorie Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11-19-01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,11-15,22 and 24-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,11-15,22,24-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

The request filed on 11/19/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/966,233 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 39-42 have been newly introduced. Claims 3, 11-15, 22, and 24-42 are under consideration by the examiner.

Response to Arguments

Applicant's arguments filed 11/19/01 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101/112

Claims 3, 11-15, 22, and 24-42 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial and credible utility or by a well established utility.

This rejection is maintained for reasons of record as applied to claims 3, 11-15, 22, and 24-38 and newly applied to claims 39-42 for the same reasons.

Claims 3, 22, 24-25, 32, and 35 are directed to isolated DNA segments encoding GDF-1 proteins. Claim 31 is directed to a complementary DNA segment. Claims 11, 26, and 33 are directed to vector containing a DNA segment encoding GDF-1. Claims 12-14, 27-29, and 36 are directed to host cells. Claims 15, 30, 34, and 37 are directed to methods of producing

recombinant GDF-1. New claims 39-42 are directed to DNA segments encoding GDF-1 proteins where the sequences hybridize under particular conditions, vectors, host cells, and methods of production, respectively. The protein products lack patentable utility for the reasons set forth below; therefore, the methods of producing the protein and vectors and hosts used therefore to make these protein products must also lack patentable utility.

Applicant previously argued that there are "at least three utilities for GDF-1 that support the claimed invention, any one of which would be adequate to provide a practical utility." The first named utility in the response is use as a specific marker for a tumor arising from a cell type that normally expresses the gene or protein. The examiner noted that no tumors have been identified in the specification as arising from a cell type that normally expresses the GDF-1 gene or protein. Thus, this is not a specific, substantial, and credible utility nor a well-known utility for GDF-1. The second named utility in the response is a marker for a particular cell lineage. Applicant references an abstract to Thibodeau et al. (1989). The examiner noted that GDF-1 has not been demonstrated to be a marker for a particular cell lineage in the specification nor is this use asserted. Thus, this is not a specific, substantial, and credible utility nor a well-known utility for GDF-1. Thibodeau et al. can be distinguished from the instant application at least because it discloses producing monoclonal antibodies and screening them to find monoclonal antibodies with unique patterns of immunoreactivity. Some antibodies found are characterized as regional, cell-lineage, cell-cycle, or extracellular material-associated markers. Again, GDF-1 has not been characterized in the specification as a marker. The third named utility in the response is a cell survival molecule in neuronal culture. The examiner noted that the specification does not positively assert that GDF-1 is a cell survival molecule in neuronal culture. As pointed to by

applicant in the response the specification states, "**If** GDF-1 possesses a similar activity...GDF-1 will **likely** prove useful..." (emphasis added). Again, the examiner maintains that the specification clearly discloses that at the time of the invention the specific biological activity associated with GDF-1 was not known. Applicant again proffered the Ebendal declaration. The examiner noted that none of the comments in the prior Office action concerning the deficiencies of the Ebendal declaration have been addressed. The examiner further noted that the Ebendal declaration does not show that GDF-1 has an activity also known to be possessed by activin at the time of the invention. Thus, use as a cell survival molecule is not a specific, substantial, and credible utility nor a well-known utility for GDF-1.

As set forth in the prior Office action, the specification discloses that the GDF-1 proteins **may** have any of a number of biological activities based upon similarity to members of the TFG-β superfamily. It is noted that these activities vary quite widely. The similarities between particular GDF-1 proteins and the TGF-β family members range from 26-52% on the amino acid level. (See specification page 12, lines 8-20.)

The specification makes clear that further experimentation is necessary to confirm the activity and uses of the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility.

Applicant's arguments concerning homology to the TGF superfamily are not persuasive as the activities of the family members are diverse and the specification does not assert a particular activity held by their claimed GDF-1 protein that is common to any or all of the family members. The Akhurst et al. (1990) reference could not be considered because it was not

attached to the response. Only a printout of the abstract with no specific publication date was provided. Even in its absence it is noted that some TGF superfamily members have diverse activities in embryonic development and some have no role in development. The particular transforming growth factors of the Akhurst et al. abstract had been well characterized for their activity. Applicant's GDF-1 had not been. Again, the specification does not assert a particular embryonic developmental activity held by their claimed GDF-1. Applicant predicted nothing in the specification other than that GDF-1 might have some activity similar to some member of the TGF superfamily. The specification makes clear that further experimentation would have been required to discover what this activity was. The Rankin (March 2000) reference is not persuasive. It was published well after the effective filing date of the instant invention (almost 10 years) and the abstract itself admits that the function of GDF-1 was not known when discovered by inventor Lee. (See abstract citations 2 and 3.) It is noted that knockout mouse were not routinely produced at the time of the invention. The specification does not appear to contemplate such an experiment nor to predict that GDF-1 was involved in development of the left-right axis in mice and expression of genes expressed downstream in development. Page 2, lines 25-29, of the specification is a general and not specific disclosure. It would not have informed one of ordinary skill in the art how to use GDF-1 at the time of the invention. Applicant's arguments concerning prenatal developmental defect screens is not persuasive as the specification does not disclose what developmental defects would have been associated with GDF-1. The subsequent assignment of other proteins to this family based on homology and discovery of their activities is not germane to the deficiencies of applicant's specification. The

fact that patents have been issued for other TGF superfamily members is also not germane. Each patent application is examined on its own merits.

Claims 3, 11-15, 22, and 24-42 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

This rejection is maintained for reasons of record as applied to claims 3, 11-15, 22, and 24-38 and newly applied to claims 39-42 for the same reasons. See also above comments.

Claims 3, 11-15, 22, and 24-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection is maintained for reasons of record as applied to claims 3, 11-15, 22, and 24-38 and newly applied to claims 39-42.

Claim 3 is directed to DNA segments encoding mouse or human GDF-1. Claim 22 is directed to mammalian GDF-1 proteins defined in an open reading frame of Figure 2 or Figure 11A or Figure 11B. Claims 24-25 and 35 specifically include sequence outside the open reading frame. Claim 31 is directed to a complementary sequence under certain hybridization conditions. All of the claims use open language.

First of all, the claim language used clearly encompasses the genomic sequences (particularly apparent in claims 24-25, 31, 35, and 39) which have not been disclosed and are thus not described. It is noted that the sequences disclosed were derived from cDNA sequences. With respect to claim 31, it is particularly noted that the Southern blot experiments in Example 5 demonstrate that even under high stringency hybridization conditions, additional bands were detected in addition to a predominant band and their sequence structure is not described. The specification clearly distinguishes them from partial digestion products.

Applicant's response does not address why the structure of the genomic sequences encompassed are described by the specification. Applicant's response does not address what the expected structure for other members of this family are nor what structural features identify a protein as a GDF-1 protein. Furthermore, as the activity of GDF-1 was not known at the time of the invention, the specification does not enable any assays for identification of GDF-1. Applicant's response does not address this point. As such, none of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Basis for new claims 39-42 is stated to be on the first paragraph of page 9. This paragraph does not disclose the limitations found in these claims nor the overall concept of sequences encoding GDF-1 proteins where the sequences hybridize to the recited cDNA sequences. Applicant is requested to point by page and line number in the specification in support of the specific limitations and overall concept of these claims.

Applicant's arguments are not persuasive with respect to the rejected claims. The specification does not describe the structure of the genomic sequences encompassed by the claims. Applicant appears to be arguing enablement issues which is not the ground of rejection. The structure or identity or other characteristics of the genomic sequences encompassed are not described by the specification.

It is believed that all pertinent arguments have been addressed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Friday from 7:00 am to 1:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028. Official FAX communications may be directed to either (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa
February 11, 2002